

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method of determining alpha-2B-adrenergic receptor function by detecting a polymorphism at a polymorphic site in a polynucleotide encoding an alpha-2B-adrenergic receptor molecule, the method comprising:
 - a. obtaining a sample of a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide; ~~and~~
 - b. detecting in the sample a polymorphism at a polymorphic site, wherein the polymorphic site is located at comprising at least one of nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or a complement thereof; and
 - c. correlating the polymorphism to an alpha-2B-adrenergic receptor function, thereby determining the function.
2. (Currently Amended) A method according to claim 1, wherein the polynucleotide polymorphism comprises SEQ ID NO: 3 or 4, or a complement thereof, at the polymorphic site.
3. (Currently Amended) A method according to claim 2, wherein the polymorphism is an insertion of ~~9~~ nine nucleotides into SEQ ID NO: 2 immediately after position 900 of SEQ ID NO: 2 at nucleotide position 901 to 909 of SEQ ID NO: 1.
4. (Currently Amended) A method according to claim 2, wherein the polymorphism is a deletion of ~~9~~ nucleotides ~~at nucleotide position 901 to 909~~ from SEQ ID NO: 1 of SEQ ID NO: 2.

5. (previously presented) A method according to claim 2, wherein the complement of the polymorphism comprises SEQ ID NO: 5 or 6.
- 6-15. (cancelled).
16. (Currently Amended) A method of genotyping an individual by genotyping a polynucleotide encoding an alpha-2B-adrenergic receptor molecule from a sample of an individual, comprising:
- a. isolating from the individual a sample having a polynucleotide encoding an alpha-2B adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide;
 - b. subjecting the polynucleotide to an incubation with at least one oligonucleotide, the at least one oligonucleotide having a nucleotide sequence that is complementary to a region of the polynucleotide, and which, when hybridized to the region permits the identification of ~~the nucleotide~~ nucleotides present at a polymorphic site of the polynucleotide, wherein the incubation is under conditions sufficient to allow specific hybridization to occur between complementary nucleic acid molecules;
 - c. permitting hybridization to occur; and
 - d. identifying the polymorphic site to obtain the genotype of the individual, wherein the polymorphic site comprises a polymorphism comprising an insertion or deletion of 9 nucleotides at nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2, wherein the at least one oligonucleotide is selected from the group consisting of

5'-AAAGCCCCACCATGGTCGGGT-3' (SEQ ID NO: 14);

5'-CTGATCGCCAAACGAGCAAC-3' (SEQ ID NO: 15);

5'-AAAAACGCCAATGACCACAG-3' (SEQ ID NO: 16);

5'-AGAAGGAGGGTGTGTTGTGGGG-3' (SEQ ID NO: 19);

5'- ACCTATAGCACCCACGCCCCT-3'(SEQ ID NO: 20);

5'-GGCCGACGCTCTTGTCTAGCC-3' (SEQ ID NO: 21);

5'-CAAGGGGTTCTTAAGATGAG-3' (SEQ ID NO: 22); and complementary sequences thereof.

17. (previously presented) The method according to claim 16, further comprising amplifying the polymorphism of the polynucleotide prior to the hybridization.
18. (cancelled)
19. (previously presented) The method according to claim 16, wherein the specific hybridization is selected from the group consisting of southern blot, dot blot, reverse dot blot, northern blot, and allele-specific oligonucleotide hybridization.
20. (Currently Amended) The method according to claim 16, wherein the at least one oligonucleotide is labeled with a label selected from the group consisting of radiolabel, fluorescent label, bioluminescent label, ~~chemiluminescent~~ chemiluminescent label, nucleic acid label, hapten label, and enzyme label.
21. (previously presented) The method according to claim 16, wherein the identity of the polymorphic site is determined by dideoxy sequencing, restriction digestion, allele-specific polymerase reaction, single-stranded conformational polymorphism analysis, genetic bit analysis, temperature gradient gel electrophoresis, ligase chain reaction, or ligase/polymerase genetic bit analysis, or random amplification of DNA.
22. (previously presented) The method according to claim 16, wherein the at least one oligonucleotide is from about 10 to about 50 nucleotides in length.

23. (withdrawn) A method of detecting a polymorphic site in a sample to determine alpha-2B-adrenergic receptor function, comprising:
- a. obtaining the sample having an alpha-2B-adrenergic receptor molecule comprising amino acid SEQ ID NO: 7 or 8 or fragment thereof and
 - b. detecting in the sample the polymorphic site at amino acid positions 294 to 309 of SEQ ID NO: 7 or 8.
24. (withdrawn) A method according to claim 23, wherein the polymorphic site comprises SEQ ID NO: 9 or 10.
25. (withdrawn) A method according to claim 23, wherein the polymorphic site is an insertion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 7.
26. (withdrawn) A method according to claim 27, wherein the polymorphic site is a deletion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 8.
27. (withdrawn) A method of detecting a polymorphic site to determine alpha-2B-adrenergic receptor function, comprising:
- a. obtaining a sample having an alpha-2B-adrenergic receptor molecule comprising amino acid SEQ ID NO: 7 or 8 or fragment thereof;
 - b. contacting the sample with an antibody specifically reactive with the polymorphic site at amino acid positions 294 to 309 of SEQ ID NO: 7 or 8; and
 - c. detecting in the sample a complex formed between the antibody and amino acid positions 294 to 309 of SEQ ID NO: 7 or 8.
28. (withdrawn) A method according to claim 27, wherein the polymorphic site is an insertion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 7.

29. (withdrawn) A method according to claim 27, wherein the polymorphic site is a deletion of 3 glutamic acids at amino acid positions 301 to 303 of SEQ ID NO: 8.
30. (cancelled)
31. (Currently Amended) A method for identifying an individual at increased risk for developing a disease associated with an alpha-2B-adrenergic receptor molecule comprising:
- a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide from the individual; and
 - b. detecting in the sample a polymorphism at a polymorphic site ~~comprising at least one of~~ located at nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or a complement thereof, wherein the polymorphism correlates to the disease, thereby identifying the individual at increased risk for the disease, wherein the disease is selected from the group consisting of cardiovascular disease, central nervous system disease, and combinations thereof.
32. (cancelled)
33. (Currently Amended) The method according to claim 31, wherein the ~~polymorphism~~ polynucleotide comprises SEQ ID NO: 3 or SEQ ID NO: 4, or a complement thereof, at the polymorphic site.
34. (Currently Amended) The method according to claim 31, wherein the polymorphism is an insertion of ~~9~~ nine nucleotides into SEQ ID NO: 2 immediately after position 900 of SEQ ID NO: 2 ~~at nucleotide position 901 to 909 of SEQ ID NO: 1.~~
35. (previously presented) The method according to claim 31, wherein the

polymorphism is a deletion of 9 nucleotides ~~at nucleotide position~~ 901 to 909 from
SEQ ID NO: 1 of SEQ ID NO: 2.

36. (previously presented) The method according to claim 33, wherein the complement of the polymorphism comprises SEQ ID NO: 5 or 6.
37. (previously presented) The method according to claim 31, wherein the alpha-2B-adrenergic receptor molecule comprises SEQ ID NO. 7 or 8 or a fragment thereof.
38. (Currently Amended) A method for diagnosing or prognosing an individual with a disease associated with an alpha-2B-adrenergic receptor molecule, comprising:
- a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or a fragment or a complement of the polynucleotide from the individual; ~~and~~
 - b. detecting in the sample a polymorphism at a polymorphic site ~~comprising at least one of~~ located at nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or a complement thereof, ~~and which correlates~~
 - c. correlating the polymorphism to the disease,
wherein the disease comprises a cardiovascular disease, a central nervous system disease, or combinations thereof.
39. (cancelled)
40. (Currently Amended) ~~A~~ The method according to claim 38, wherein the ~~polymorphism~~ polynucleotide comprises SEQ ID NO: 3 or SEQ ID NO: 4, or a complement thereof, at the polymorphic site.
41. (Currently Amended) The method according to claim 38, wherein the polymorphism is an insertion of 9 nine nucleotides into SEQ ID NO: 2 immediately after position

900 of SEQ ID NO: 2 at nucleotide position 901 to 909 of SEQ ID NO: 1.

42. (Currently Amended) The method according to claim 38, wherein the polymorphism is a deletion of 9 nucleotides ~~at nucleotide position 901 to 909~~ from SEQ ID NO: 1 ~~of SEQ ID NO: 2.~~
43. (previously presented) The method according to claim 40, wherein the complement of the polymorphism comprises SEQ ID NO: 5 or 6.
44. (previously presented) The method according to claim 38, wherein the alpha-2B adrenergic receptor molecule comprises SEQ ID NO: 7 or 8 or a fragment thereof.
45. (withdrawn) A method of predicting an individual's response to an agonist or antagonist, comprising:
- a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement of the polynucleotide from the individual;
 - b. detecting in the sample a polymorphic site comprising nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or fragment or complement thereof; and
 - c. correlating the polymorphic site to a predetermined response thereby predicting the individual's response to the agonist or antagonist.
46. (withdrawn) A method according to claim 45, wherein the alpha-2B adrenergic receptor molecule comprises SEQ ID NOS. 7 or 8 or fragment thereof.
47. (withdrawn) A method according to claim 45, wherein the agonist is an alpha-2B adrenergic receptor agonist.

48. (withdrawn) A method according to claim 45, wherein the antagonist is an alpha-2B adrenergic receptor antagonist.
49. (withdrawn) A method according to claim 47, wherein the alpha-2B adrenergic receptor agonist is an agonist selected from the group consisting of epinephrine, norepinephrine, clonidine, oxymetazoline, guanabenz, UK14304, BHT933 and combinations thereof.
50. (withdrawn) A method according to claim 48, wherein the alpha-2B adrenergic receptor antagonist is an antagonist selected from the group consisting of yohimbine, prazosin, ARC 239, rauwolscline, idazoxan, tolazoline, phentolamine and combinations thereof.
51. (withdrawn) A method according to claim 45, wherein the predetermined response to the agonist or antagonist is correlated to adenylyl cyclase, MAP kinase activity, phosphorylation or inositol phosphate levels.
52. (withdrawn) A method according to claim 45, wherein the individual is homozygous for SEQ ID NO: 2 and exhibits a decreased response to the alpha-2B adrenergic receptor agonist.
53. (withdrawn) A method according to claim 45, wherein the individual's response is desensitization to the agonist or antagonist.
54. (withdrawn) A method according to claim 47, wherein the individual's response is desensitization to the alpha-2B-adrenergic receptor agonist.
55. (withdrawn) A method for selecting an appropriate pharmaceutical composition to administer to an individual having a disease associated with an alpha-2B adrenergic receptor molecule, comprising:
 - a. obtaining a sample having a polynucleotide encoding an alpha-2B-adrenergic receptor molecule comprising SEQ ID NO: 1 or 2 or fragment or complement of the

polynucleotide from the individual;

- b. detecting in the sample a polymorphic site comprising nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or fragment or complement thereof; and
- c. selecting the appropriate pharmaceutical composition based on the polymorphic site present.

- 56. (withdrawn) A method of claim 55, wherein the disease is a cardiovascular disease, a central nervous system disease or combinations thereof.
- 57. (withdrawn) A method according to claim 55, wherein the alpha-2B-adrenergic receptor molecule comprises SEQ ID NO. 7 or 8 or fragment thereof.
- 58. (withdrawn) A method according to claim 55, wherein the pharmaceutical composition is an alpha-2B-adrenergic receptor agonist or antagonist.
- 59. (withdrawn) A method according to claim 58, wherein the alpha-2B-adrenergic receptor agonist is an agonist selected from the group consisting of epinephrine, norepinephrine, clonidine, oxymetazoline, guanabenz, UK14304, BHT933, and combinations thereof.
- 60. (withdrawn) A method according to claim 58, wherein the alpha-2B adrenergic receptor antagonist is an antagonist selected from the group consisting of yohimbine, prazosin, ARC 239, rauwolscine, idazoxan, tolazoline, phentolamine and combinations thereof.
- 61. (withdrawn) A method according to claim 58, wherein the appropriate pharmaceutical composition to administer is correlated to adenyly cyclase, MAP kinase, phosphorylation or inositol phosphate activity.
- 62. (withdrawn) A method according to claim 55, wherein the individual is homozygous for SEQ ID NO: 2 and exhibits a decreased response to the alpha-2B

adrenergic receptor agonist.

63. (Currently Amended) A method of determining alpha-2B-adrenergic receptor function by indirectly detecting a polymorphism at a polymorphic site in a polynucleotide encoding an alpha-2B-adrenergic receptor molecule, the method comprising:
- a. obtaining a sample comprising a polynucleotide encoding an alpha-2B-adrenergic receptor molecule, wherein the polynucleotide, or a fragment or a complement thereof, comprises SEQ ID NO: 1 or 2 ; and
 - b. indirectly detecting in the sample the polymorphism at the polymorphic site located at comprising at least one of nucleotide positions 901 to 909 of SEQ ID NO: 1 or 2 or a complement thereof; and
 - c. correlating the polymorphism to a predetermined alpha-2B-adrenergic receptor function, thereby determining the function.
64. (withdrawn) A method of detecting a polymorphic site in a sample to determine alpha-2B-adrenergic receptor function, comprising:
- a. obtaining the sample having an alpha-2B-adrenergic receptor molecule comprising amino acid SEQ ID NO: 7 or 8 or fragment thereof; and
 - b. indirectly detecting in the sample the polymorphic site at amino acid positions 294 to 309 of SEQ ID NO: 7 or 8.
65. (New) The method of determining alpha-2B-adrenergic receptor function by detecting a polymorphism at a polymorphic site in a polynucleotide encoding an alpha-2B-adrenergic receptor molecule as recited in claim 1, wherein the function comprises mediation of: adenylyl cyclase; MAP kinase; G protein receptor interaction; inositol phosphate; phosphorylation; receptor desensitization; and combinations thereof.

66. (New) The method as recited in claim 65 wherein the function comprises phosphorylation.
67. (New) The method as recited in claim 66, wherein the phosphorylation comprises agonist promoted phosphorylation by G-protein coupled receptor kinases.